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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/835,381	04/17/01	SUGA	M 206018US0

022850 HM12/0828
OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT
FOURTH FLOOR
1755 JEFFERSON DAVIS HIGHWAY
ARLINGTON VA 22202

EXAMINER	
FRONDA, C	
ART UNIT	PAPER NUMBER
1652	5

DATE MAILED: 08/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/835,381	Suga et al.
Examiner	**Art Unit**
Christian L. Fronda	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-4 is/are pending in the application.

4a) Of the above, claim(s) 4 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-3 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-3, in Paper No. 4 is acknowledged. The traversal is on the ground(s) that the restriction requirement is improper and that a search of all the claims would not be a serious burden.

This is not found persuasive because as stated in the Office Action dated 7/20/2001 (paper no. 2), the invention of Group I is related to the invention of Group II as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the process for using the product as claimed can be practiced with another materially different product such as using chemical reagents in a chemical synthesis or preparation of L-arginine. A search of all the inventions in the patent literature and the non-patent literature cannot be made without serious burden because the inventions require separate searches that have different limits, boundaries, scope, and subject matter.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-3 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-3 are rejected under 35 U.S.C. 101 because the claims are directed toward non-statutory subject matter. These claims encompass any naturally occurring species variants of coryneform bacteria which have a mutation that renders the arginine repressor defective. Hence, the claims are directed toward non-statutory subject matter.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to any coryneform bacteria having any mutation in any gene in which an "arginine repressor does not function in a normal manner", any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence of SEQ ID NO: 18 or an amino acid sequence "showing homology" to SEQ ID NO: 18.

However, the specification discloses only a single representative species encompassed by these claims: a *Brevibacterium lactofermentum* strain containing a disruption of the *argR* gene, wherein said *argR* gene consists of the nucleotide sequence of SEQ ID NO: 17 and said strain is identified as strain AJ13029ΔR. There is no disclosure of any particular structure to function/activity relationship in the single disclosed *argR* gene consisting of SEQ ID NO: 17 which can be used to identify any other gene encoding any arginine repressor of any structure from any other species of coryneform bacteria. The specification also fails to describe additional representative species of coryneform bacteria encompassed by the claims by any identifying structural characteristics or properties other than the strain AJ13029ΔR having a disruption in the *argR* gene consisting of the nucleotide sequence of SEQ ID NO: 17 which encodes the arginine repressor for which no predictability of structure is apparent.

Given the lack of additional representative species and written description of any coryneform bacterium in which an "arginine repressor does not function in a normal manner", any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID NO: 18, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

7. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *Brevibacterium lactofermentum* strain containing a disruption of the *argR* gene, wherein said *argR* gene consists of the nucleotide sequence of SEQ ID NO: 17 and said strain is identified as strain AJ13029ΔR, does not reasonably provide enablement for any coryneform bacterium having any mutation in any gene in which an "arginine repressor does not function in a normal manner", any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID NO: 18. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any coryneform bacterium having any mutation in any gene in which an "arginine repressor does not function in a normal manner", any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID NO: 18. The specification provides guidance and examples in making a *Brevibacterium lactofermentum* strain containing a disruption of the *argR* gene, wherein said *argR* gene consists of the nucleotide sequence of SEQ ID NO: 17 and said strain is identified as strain AJ13029ΔR.

While molecular biological techniques and genetic manipulation techniques are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific coryneform bacterium having any mutation in any gene in which an "arginine repressor does not function in a normal manner", coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID NO: 18 is lacking. Thus, searching for any coryneform bacterium having any mutation in any gene in which an "arginine repressor does not function in a normal manner", any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or any coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID

NO: 18 is well outside the realm of routine experimentation and predictability in the art of success is extremely low. In addition, searching for the all the specific enzymes or proteins which affect or influence the function of the arginine repressor and determining whether mutating said enzyme or proteins would result in an defective arginine repressor is well outside the realm of routine experimentation.

The amount of experimentation to determine the specific coryneform bacterium having any mutation in any gene in which an "arginine repressor does not function in a normal manner", coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor, or coryneform bacteria which has a disrupting of the gene consisting of any nucleotide sequence encoding an arginine repressor having an amino acid sequence "showing homology" to SEQ ID NO: 18 is enormous. Such experimentation entails selecting a species of coryneform bacteria out of a vast number of species, isolating the arginine repressor from the selected species, obtaining the amino acid sequence of the isolated arginine repressor and determining if its amino acid sequence shows "homology" to the amino acid sequence of SEQ ID NO: 18, obtaining the nucleotide sequence encoding the arginine repressor by screening genomic libraries of the selected species of coryneform bacteria, selecting a specific type of mutation out of a vast number of mutations to perform on the selected species such as disruption of the gene encoding the arginine repressor in the selected coryneform bacteria species, and determining whether the mutation results in a coryneform bacteria species which produces and accumulates more L-arginine than the wild type coryneform bacteria species.

Since routine experimentation in the art does not include the enormous amount of experimentation stated above where the expectation of obtaining the desired species of coryneform bacteria is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific species of coryneform bacteria having an arginine repressor and the specific mutation to perform to create a strain that produces and accumulates more L-arginine than the wild type bacteria, the nucleotide sequence of the gene encoding the arginine repressor, the amino acid sequence of the arginine repressor, and the type of mutation. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1 and 2, the phrase "does not function in a normal manner" renders the claim indefinite because the specification does not define the phrase and one of skill in the art cannot determine the metes and bounds of the claimed invention. Furthermore, in claim 2, the phrase "a gene coding for the arginine repressor" is indefinite because the specific nucleotide sequence of the claimed gene is not known.

In claim 3, the phrase "showing homology to the amino acid sequence" renders the claim indefinite because the specification does not defined "homology" and one of skill in the art cannot determine the metes and bounds of the claimed invention.

Conclusion

10. No claim is allowed.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Makarova et al. teach the binding sites for the arginine repressor in bacteria (see entire publication).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600